AMENDMENTS TO THE CLAIMS

Listing of Claims:

This listing of claims is to replace all previous listings.

1-76. (Canceled)

77. A method for generating and analyzing multi-factorial biological response profiles, comprising

a) exposing each member of a plurality of expression control sequences, each of which is operatively linked to a heterologous reporter sequence, independently, to at least about three stimuli from a first set of stimuli, wherein at least about two of the stimuli in said first set of stimuli are, optionally, combined in an intra-set combinatorial fashion,

b) detecting a first category of responses of said expression control sequences to said stimuli, and

c) generating a response profile for each of said expression control sequences.

78. The method of claim 77, wherein at least about two of the stimuli in said first set of stimuli are combined in an intra-set combinatorial fashion.

79. The method of claim 77, further comprising

d) exposing each of said members of the plurality of expression control sequences, independently, to one or more additional sets of stimuli, optionally wherein at least about two of the stimuli in each of said additional sets of stimuli are combined in an intra-set combinatorial fashion,

in an inter-set combinatorial fashion with set first set of stimuli,

e) detecting the first category of responses of said expression control sequences to the stimuli in d), and

f) generating a response profile for each of said expression control sequences, which includes the responses detected in b) and in e).

80. The method of claim 79, wherein at least about two of the stimuli in each of said additional sets of stimuli are combined in an intra-set combinatorial fashion.

81.   The method of claim 79, wherein said members of the plurality of expression control sequences are exposed, independently, to one additional set of stimuli.

82.   The method of claim 77, further comprising detecting one or more different categories of responses of said expression control sequences in a) to said stimuli, and combining those responses with the responses detected in b) to generate a response profile for each of said expression control sequences.

83.   The method of claim 79, further comprising detecting one or more different categories of responses of said expression control sequences in a) to said stimuli, and combining those responses with the responses detected in e) to generate a response profile for each of said expression control sequences.

84.   The method of claim 77, wherein the response of the expression control sequences to the stimuli is one or more of the following categories:

    a) levels of RNA produced in response to the stimuli,

    b) levels of proteins translated from said RNA,

    c) levels of post-translational protein modification,

    d) movement of an RNA polymerase molecule along a DNA template (as determined by nuclear run-on analysis) in response to the stimuli, and/or

    e) the formation of protein-DNA complexes (as determined by kinetic analysis) in response to the stimuli, and/or

    f) changes in lipid membrane composition,

    h) or a combination thereof.

85.   The method of claim 84, further wherein the response of the expression control sequences to the stimuli is

    i) responses detected at one or more different time points following the exposure of each of said expression control sequences to one of more of the stimuli in a) through h), and/or

j) responses to one or more different amounts (concentrations) or one of more of the stimuli.

86.   The method of claim 79, wherein the stimuli in the first set and the stimuli in each of the additional sets represent different categories of stimuli.

87.   The method of claim 86, wherein the different categories are:

a) agents that act at the surface of a cell vs. agents that function within a cell,

b) agents that exhibit different mechanisms of action,

c) agents that have different chemical structures vs. agents within a particular chemical class that differ from one another,

d) agents that are produced within a cell vs. agents that are introduced directly into a cell,

e) agents having a known mechanism of action on an expression control sequence vs. agents not having a known mechanism,

f) agents having a known effect on the expression control sequence vs. test agents,

g) agents known to have an effect on at least one of the expression control sequences vs. agents not known to have an effect on any of those expression control sequences,

h) naturally occurring agents vs. artificially generated molecules, and/or

i) physical agents vs. environmental stimuli, or

j) a combination thereof.

88.   The method of claim 77, wherein the response profiles are raw profiles, and generating the raw profiles comprises inputting the responses into a database, thereby generating a database which comprises a raw profile for each of the expression control sequences.

89.   The method of claim 77, wherein the response profiles are processed profiles, and generating the processed profiles comprises

inputting the responses into a database, thereby generating a database which comprises a raw profile for each of the expression control sequences, and

processing the data base comprising the raw profiles with a multivariate statistical method.

90. The method of claim 89, wherein the multivariate statistical method is

i) principal component analysis,

ii) hierarchical clustering,

iii) unsupervised neural networks, and/or

iv) ANOVA studies,

or a combination thereof.

91. The method of claim 89, wherein the responses are inputted into a computer.

92. The method of claim 89, further comprising displaying the processed profiles.

93. The method of claim 77, which is a high throughput method.

94. A method of claim 77, which is

a) a method for determining the type of an unknown stimulus,

b) a method for identifying/characterizing a modulatory or co-modulatory agent,

c) a method for identifying the cellular pathway affected by an agent,

d) a method for determining whether a drug candidate has an activity similar to a known drug,

e) a method for identifying a regulatory pathway, control point or therapeutic target,

f) a method for studying a combinatorial drug strategy in a pre-clinical setting,

g) a method for identifying a cell or organism that is sensitive or resistant to a drug composition,

h) a method for determining if a sample is susceptible to, or likely to benefit from, a particular treatment, or

i) a method for determining if an agent is toxic.

95. The method of claim 77, wherein the plurality of expression control sequences exhibit coordinated biological activity.

96. A computer-implemented method for generating and analyzing multi-factorial biological response profiles, comprising

a) exposing each member of a plurality of expression control sequences, each of which is operatively linked to a heterologous expression control sequence, independently, to

at least about three stimuli from a first set of stimuli, wherein at least about two (e.g., at least about three) of the stimuli in said first set of stimuli are combined in an intra-set combinatorial fashion, and to

at least about three stimuli from a second set of stimuli, wherein at least about two of the stimuli in said second set of stimuli are optionally combined in an intra-set combinatorial fashion,

in an inter-set combinatorial fashion,

b) detecting and inputting into a computer responses of said expression control sequences to said stimuli, thereby generating a database which comprises a raw profile for each of the expression control sequences,

c) processing the data base comprising the raw profiles with

i) principal component analysis,

ii) hierarchical clustering,

iii) unsupervised neural networks, and/or

v) ANOVA studies,

or a combination thereof, and, optionally,

d) displaying the processed profiles.

97. A kit, comprising

(1) a plurality of recombinant constructs, each of which comprises an expression control sequence from a coordinated system of interest operatively linked to a reporter,

(2) at least three about agents from a first set of agents that are known or predicted to act on at least one of said expression control sequences, and

(3) at least about three agents from a second set of agents,

wherein said at least about three agents from said first and second sets of agents are combined in an inter-set combinatorial fashion

and, optionally,

(3) an electroporation device suitable for electroporating said recombinant constructs into suitable cells; and/or

(4) instructions for how to detect the effects of the agents on the expression control sequences.

98.   A computer system for generating and analyzing multi-factorial biological response profiles, comprising

a) means for inputting responses into a database, wherein said responses are generated by

i) exposing each member of a plurality of expression control sequences, each of which is operatively linked to a heterologous expression control sequence, independently, to

at least about three stimuli from a first set of stimuli, wherein at least two of the stimuli in said first set of stimuli are combined in an intra-set combinatorial fashion, and to

at least about three stimuli from a second set of stimuli, wherein at least about two of the stimuli in said second set of stimuli are optionally combined in an intra-set combinatorial fashion,

in an inter-set combinatorial fashion, and

ii) detecting the responses of said biological entities to said stimuli;

b) means for analyzing said inputted responses; and, optionally,

c) means for displaying the analyzed responses.

99.   A computer-readable storage medium storing computer-readable program code for causing a computer to perform the following steps:

a) retrieving responses generated by

i) exposing each member of a plurality of expression control sequences, each of which is operatively linked to a heterologous expression control sequence, independently, to

at least about three stimuli from a first set of stimuli, wherein at least two (*e.g.*, at least about three) of the stimuli in said first set of stimuli are combined in an intra-set combinatorial fashion, and to

at least about three stimuli from a second set of stimuli, wherein at least about two (*e.g.*, at least about three) of the stimuli in said second set of stimuli are optionally combined in an intra-set combinatorial fashion,

in an inter-set combinatorial fashion, and

ii) detecting the responses of said biological entities to said stimuli,

b) processing the retrieved responses with a multivariate statistical method and, optionally,

c) displaying the processed responses.